Modification/Improvement of the Wurster process for drying or coating sensitive bioactive materials

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The Wurster process is a coating technique that is well suited to uniformly coat or encapsulate individual particulate materials. However, its use for coating sensitive bioactive compounds is often limited because of the potential risks of degradation during operations.
In order to avoid a loss of integrity of such material during the process, we proposed some modifications of the equipment. The standard and modified systems were compared using probiotic microorganisms as model for sensitive material.
The results obtained for the pressure drop measurements at various air flow rates are rapresented by a 4 distinct states of fluidization for the conventional equipment and only 3 states (S1, S2 and S3) for the modified one.
Our results demonstrated that the modifications carried out led to more gentle operating conditions, resulting in an enhanced cell survival during the coating process.

KEY WORDS: Wurster process - Fluidization - Coating - Sensitive materials - Drying.

The Wurster process is an industry recognized coating technique for precision application of film coat to particulate materials such as powders, crystals, or granules. This technology is used in many different fields, including pharmacy, agriculture, and food. The Wurster Process is characterized by the location of a spray nozzle at the bottom of a fluidized bed of solid particles. The particles are suspended in the fluidizing air stream that is designed to induce a cyclic flow of the particles (Figure 1A). The nozzle sprays an atomized flow of coating solution, suspension, or other coating vehicle. The atomized droplets collide with the particles as they are carried away from the nozzle. The temperature of the fluidizing air is set to appropriately evaporate solution or suspension solvent or solidify the coating material shortly after colliding with the particles. All coating solids are left on the particles as a part of the developing film or coating. This process is continued until each particle is coated uniformly to the desired film thickness.

In the conventional Wurster process, the particles spend most of their time in the annular zone, waiting for their entrainment in the spout zone (pulverization zone). This may cause an overheating of the particles in this region of the reactor, which is not desirable when coating thermosensitive materials.[1] This major drawback has been initially pointed out by Poncelet *et al.*[2] who proposed several ways of modifying the equipment in order to avoid a temperature increase in the annular zone. In one of the modifications proposed, the fluidizing air passes only through the spout region, entraining the particles along the insert (Figure 1B). The fluidized air bed system thus obtained behaves like a spouted bed equipped with a draft tube.

The main objective of this work was to characterize and compare the fluidization regime and the tem-

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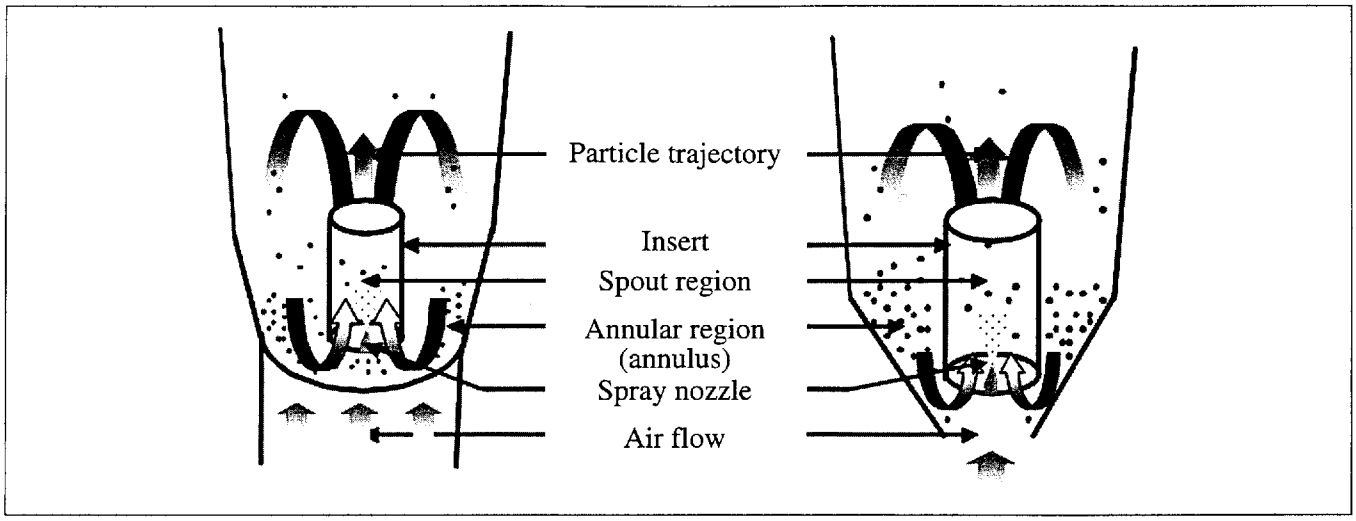

Figure 1.—Schematic representation of the Wurster coating process with A) the conventional equipment and B) the modified equipment.

perature profile obtained during the Wurster process using the conventional equipment and the modified system described above. In addition, the effect of the modification of the conventional equipment on the survival of sensitive probiotic microorganisms during drying (atomization of the cell suspension on a fluidized inert carrier) was also determined.

Materials and methods

Core material and coating solutions

Microcrystalline cellulose (MCC) particles with a density of 1 395 kg/m^3 and sizes ranging from 500 to 700 µm were obtained from IPC (Dresden, Germany) and used as core material. The particles were autoclaved at 120 °C for 15 min when used for drying of microorganisms.

Coating solutions containing skim milk (40% w/w) and sucrose (10% w/w) were prepared in distilled water and filter-sterilized when used for drying of microorganisms.

Fluidized bed equipment

All the coating experiments were performed in the bottom spray reactor of the Uni Glatt (Glatt GmbH, Binzen, Germany). For the modified equipment, the bottom of the reactor was adapted in order to facilitate the displacement of the particles to the spout region in absence of fluidizing air in the annular zone (Figure 1B). To this end, a hollow conical disc was manufactured in the laboratory and positioned in the bottom of the reactor.

Pressure drop and temperature measurements

The pressure drop was measured at different air flow rates using two transmitters of differential pressure (Model P92, Etoile International, France) that were placed between the air entrance and the top of the annular bed as previously described by El mafadi *et al.*[3] (Figure 2).

The temperature profile in the standard and modified reactor during the pulverization of distilled water on microcrystalline cellulose particles was determined using thermocouples located in the annular bed and the coating chamber. Distilled water was sprayed at 10 g/min onto 500 g of fluidized MCC. The fluidization air flow rate was set at 100 m3/h and the inlet temperature at 65 °C.

Drying of microorganisms

Freeze-dried powders of Lactobacillus casei Lc1 (CNCM MA43/6V) and Lactobacillus acidophilus R0052 (CNCM I-1722 OI 5062) were obtained from Lesaffre International (Marcq-en-Barœul, France) and Lallemand SAS (Blagnac, France), respectively, and used as models for sensitive material. For each culture, a given amount of powder was added aseptically to

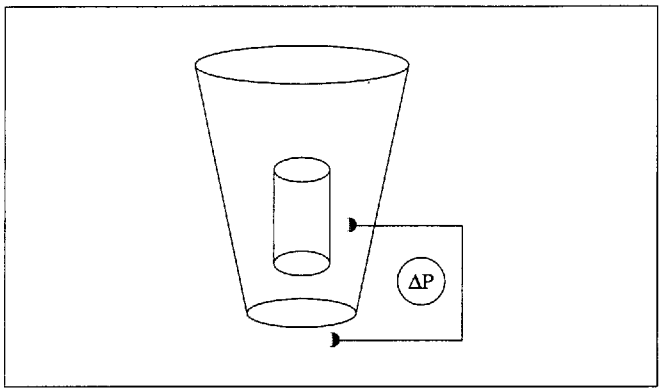

Figure 2.—Emplacement of pressure captors for pressure drop measurement.

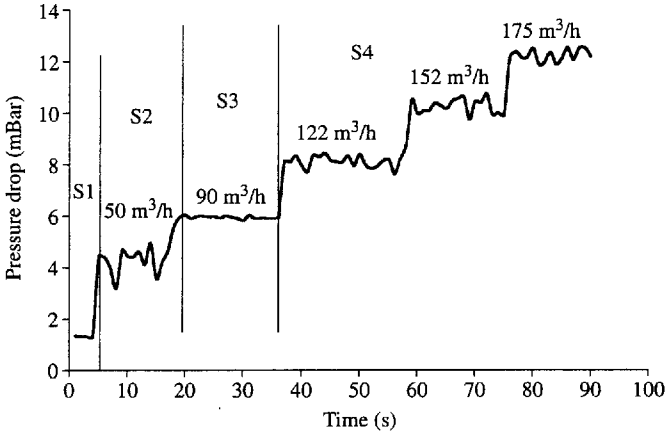

Figure 3.—Pressure drop in the annular bed according to the air flow rate in the conventional equipment.

the sterile coating solution (50% w/w solids) in order to get a final concentration of 2x10E9 cfu/mL. Once the rehydration was completed (15 min), the cell suspension was sprayed at an inlet air temperature of 60 °C onto 500 g of fluidized MCC particles using both the standard and the modified fluidized bed equipment. The fluidization air flow rate was set at 100 m³/h, and the atomization air pressure was 2 bars. Coating of the MCC particles with the cell suspension was carried out until a 20% weight gain of the particles was reached (30-35 min, theoretical final cell concentration of 6x10E8 cfu/g). Survival of the probiotic cultures was compared after resuspension of the coated MCC particles in sterile 0.9% saline during 15 min (complete dissolution of the coating) and cell enumeration. Viable cell counts were determined in duplicate on MRS agar using the pour plate method. The plates were incubated at 37 °C for 48 h in anaerobic jars with the Anaerocult system (Merck, Darmstadt, Germany). Each coating experiment was performed in triplicate and means are reported.

Results

Pressure drop measurement: fluidization control

Recording pressure drop can be a good indicator to determine optimal parameters for a good fluidization in the Wurster process.

The results obtained for the pressure drop measurements at various air flow rates are presented in Figure 3 for the conventional equipment and Figure 4 for the modified one.

Conventional equipment

In a standard fluidized bed system, the particles remain static at very low air flow rate, without any visible movement (packed bed). When increasing the air flow rate, the particles move slightly and an expansion of the bed can be observed until a fluidized state is reached. As the air flow rate increases, the fluidization of the particles becomes more violent and some bubbles, which explode at the surface of the bed, can be seen. This state is called the bubbling fluidization. Finally, for very high air flow rates, the particles leave the bed and the transported bed mode is reached.

For the conventional equipment, 4 distinct states of fluidization can be observed (Figure 3). The S2 and S4 states are characterized by important pressure drop fluctuations, whereas the pressure drop for the S1 and S3 states is very stable. The S1 state refers to a packed bed as described above, which means that no transport of particles can be observed and the pressure drop is then stable. When increasing the air flow rate, some particles start to move up into the insert and others are entrained from the annulus, but not at the same speed, which causes some fluctuations of pressure drop (S2). A further increase in the air flow rate improves the transport of the particles, which becomes more uniform. Thus, the fluctuations observed in the S2 state disappear and the stable state of fluidization is attained. For higher air flow rates, fluctuations of the pressure drop are more important and correspond to a vigorous fluidization of the particles in the annular bed (S4).

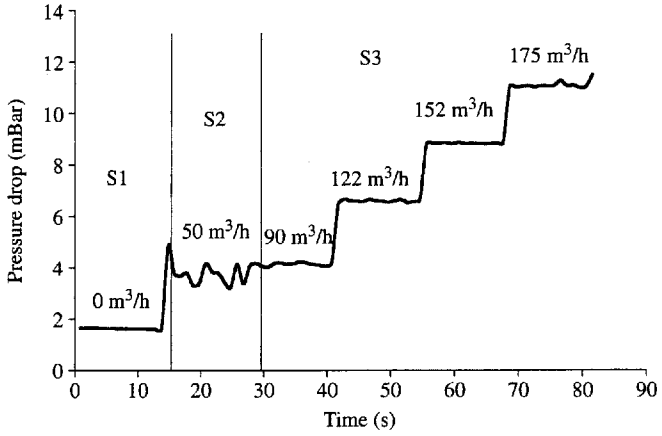

Figure 4.—Pressure drop in the annular bed according to the air flow rate in the modified equipment.

MODIFIED EQUIPMENT

For the modified equipment, only 3 states (S1, S2 and S3) were observed (Figure 4). Once suitable conditions of fluidization are reached (S3), the pressure drop remains stable, even if the air flow rate is increased. The absence of the S4 state in this case can be explained by the absence of the vigorous fluidization observed with the conventional equipment. The fluidizing air passes only through the spout region without destabilizing the bed in the annular region, leaving the transport of the particles uniform without any fluctuation of the pressure drop.

In conclusion, the modification of the equipment proposed improves the stability of the fluidization process.

Temperature profile during coating

Figure 5 shows the temperature profile results obtained using both conventional and modified equipments under conditions described below in "Materials and methods".

In the case of the conventional equipment, the temperature in the annular bed is 15 °C higher than that of the coating chamber (Figure 5A). This difference can be explained by the fact that air passing through the annular bed increases the temperature in this region of the reactor in the absence of liquid feed. The temperature in the annular bed, which is very similar to the temperature of the particles, remains too high for coating of heat-sensitive materials.

In the case of the modified equipment, the temperature in the annular bed drops compared with that measured with the conventional equipment, and the difference with the temperature of the coating chamber becomes very slight (-2 °C).

In conclusion, the modification of the equipment avoids an overheat of the particles in the annular space, which could be advantageous for coating or drying sensitive bioactive compounds and limiting the potential risks of degradation during operations.

Drying of microorganisms

According to the results presented in Table I, the survival rate during the coating process was increased by about 8-14% using the modified fluidized bed equipment. Final cell concentrations were 34% and 102% higher for *L. casei* Lc1 and *L. acidophilus* R0052, respectively. This improvement is directly related to the

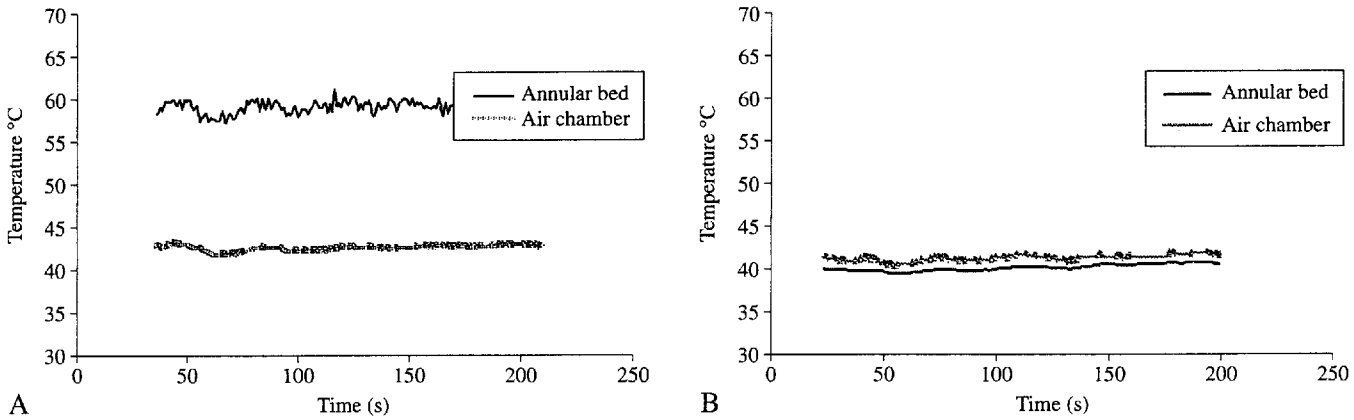

Figure 5.—Temperature profiles obtained with A) the conventional equipment and B) the modified equipment.

TABLE I.—*Survival rate of* Lactobacillus casei *Lc 1 and* Lactobacillus acidophilus *R0052 during drying (anatomization of the cell suspension on a fluidized inert carrier) using the conventional and the modified fluidized bed equipment.*

Probiotic strain	Survival rate with the conventional equipment (%)	Survival rate with the modified equipment (%)	Increase of the final cell concentration (%)
L. casei Lc1	40.1±6.9	53.6±7.2	34
L. acidophilus R0052	7.6±1.3	15.3±1.4	102

lower temperature obtained in the annular bed with the modified equipment, as described previously.

The technological properties of probiotic bacteria, particularly heat resistance, varied considerably from strain to strain.[4] The high survival rates observed for *L. casei* Lc1 during drying with both systems (40.1% and 53.6% with the conventional and the modified equipment, respectively) indicate that this culture is relatively thermoresistant. The modification of the fluidized bed equipment had a more significant effect on the final cell concentration for *L. acidophilus* R0052 (102% increase *vs* 34% for *L. casei* Lc1), probably because this strain is more heat sensitive intrinsically. However the survival rate remains relatively low in this case. Loss of viability during drying in a fluidized bed is not only due to dehydration and thermal inactivation but also to collisions between particles and application of a high mechanical stress, which often leads to irreversible cellular damages and/or a higher sensitivity to additional stresses (including temperature).

Concentrated dried cultures with acceptable residual viability were obtained using the modified fluidized bed equipment. Survival rate could be further improved by optimizing the formulation of the coating solution, adjusting the inlet air temperature and the fluidization air flow rate, and reducing the residence time in the reactor.

Discussion and conclusions

A modification of the Wurster coating process was proposed to encapsulate sensitive bioactive compounds. The modified equipment is characterized by the presence of a hollow conical disc in the bottom of the reactor, which prevents the passage of the fluidizing air in the annular section. This modification ensures a fast recirculation of the particles towards the spout zone where the contact between the particles and the atomized droplets should be done.

Using the pressure drop method, it was demonstrated that the fluidization of particles in the modified equipment is more stable, which leads to a uniform circulation of the particles to be coated. In addition, the determination of the temperature profile in both systems showed that the modification of the equipment avoid an overheating of particles in the annular bed observed. Therefore, the technology developed in this study can potentially be used for coating or drying heat-sensitive materials.

The results obtained with the two lactobacilli strains used in this study demonstrated that the modification carried out led to more gentle operating conditions, resulting in an enhanced cell survival during the coating process. Further studies are under way to validate the method with other probiotic cultures and demonstrate its effectiveness for encapsulating sensitive bacteria (coating of freeze-dried bacteria used as core material). Future work will include the optimization of the design of the modified equipment described in this study.

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